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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,944	08/08/2001	Douglas C. Harnish	0630/1G704US2	2000

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DARBY & DARBY P.C.
P.O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,944	HARNISH ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The amendment and response filed on 3/17/2003 is acknowledged. Applicant's request for rejoining the process is acknowledged. When the claims drawn to the product is allowable, the process claims including all the limitations of allowable subject matter would be rejoined.

Claim 1 is amended. Claims 1-25 are pending and claims 12-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) for reason of record.

This application contains claims 12-24 drawn to an invention nonelected with traverse in the reply filed on 3/26/2003. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-11, and 25 are under consideration.

This Office action contains a new ground of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims 1-11, and 25 under 35 U.S.C. 103(a) as being unpatentable over Harnish et al (1998, J. Biol. Chem. vol. 273, pages 9270-8) and Ameis et al (1990, J. Biol. Chem. vol. 265, pages 6552-5) in view of Norris et al (1995, J. Biol. Chem. vol. 270, pages 22777-82), US Pat 5,908,859 (June 1, 1999, or Dichek et al (1998, J. Biol. Chem. vol. 273, pages 1896-903), and

further in view of Kwok et al (1994, Nature, vol. 270, pages 177-8, abstract only) is **withdrawn** in view of the newly available art submitted in the IDS filed on 03/17/2004.

The Following Is New Ground of Rejection

Claim Rejections - 35 USC § 103

Claims 1-11, and 25 are under 35 U.S.C. 103(a) as being unpatentable over Harnish et al of record (1998, J. Biol. Chem. vol. 273, pages 9270-8) and Ameis et al of record (1990, J. Biol. Chem. vol. 265, pages 6552-5) in view of either Landschultz et al., (CA of IDS filed on 03/17/04) or Birkenmeier et al., (CB of IDS filed on 03/17/04), and further in view of Norris et al of record (1995, J. Biol. Chem. vol. 270, pages 22777-82), US Pat 5,908,859 of record (June 1, 1999, or Dichek et al of record (1998, J. Biol. Chem. vol. 273, pages 1896-903).

Claims 1-10 and 25 are interpreted as drawn to recombinant cell (more specifically a hepatocarcinoma cell in claim 9, **HepG2** cell in claim 10) containing 3 DNA constructs, i.e. 1) **DNA construct expressing a estrogen receptor** (more specifically human one in claim 2, human estrogen receptor alpha (ER-alpha) in claim 3); 2) **DNA construct expressing a transcription coactivator C/EBP**; 3) **a reporter construct linking various art-known reporters listed in** claim 7 (more specifically luciferase in claim 8) to **hepatic lipase promoter/enhancer** that **contains CCAAT element** (more specifically –1557 to +43 of human HL gene in claim 6). Claim 11 is interpreted as drawn to the recombinant cell of claim 1 for screening useful compounds affecting the ERalpha and/or C/EBP dependent transcription activation of hepatic lipase

promoter/enhancer in multi-well format capable of detecting the reporter being used. In summary, the claims are drawn to **a recombinant cell per se** with 3 vectors encoding two proteins i.e. a known- promoter linked to a known reporter, encoding a coactivator of transcription (estrogen receptor), and transcription enhancer binding protein of C/EBP.

The primary references (Harnish et al and Ameis et al, both of record) teach all the materials and/or technology necessary to make and use **a transformed cell**. Ameis et al teach at Fig. 3 **a human HL promoter/enhancer (–1557 to +43)**, which contains CCAAT element. Harnish et al teach **HepG2 cells** and other cells, **a DNA construct expressing a estrogen receptor, more specifically human ER-alpha, the ER-alpha used is a human origin, a reporter construct linking various art-known reporters to a promoter/enhancer of interest** in the case of Harnish et al, apoAI (Note the entire article, especially Materials and Methods section at page 9271). Harnish et al., teach how to use a vector expressing ER-alpha for regulating transcription activity of a reporter construct linking various art-known reporters to a promoter/enhancer of interest. See the paragraph bridging page 9270-1. Harnish et al also teach why HepG2 is used in ER-alpha dependent transcription study. See page 9271, Right column, 2nd paragraph.

The primary references do not teach a vector encoding C/EBP transcription factor capable of binding CCAAT element that is located the HL gene.

However, either one of Landschultz et al., or Birkenmeier et al., (CB of IDS filed on 03/17/04) teach how to make a vector encoding C/EBP transcription factor capable of binding CCAAT element that is located the HL gene. Birkenmeier et al (see abstract, for example) teach C/EBP binds to CCAAT/enhancer binding protein (C/EBP) recited in the amended base claim 1.

The primary references and the secondary references do not teach why one of ordinary skill would put the three vectors together in a cell.

However, any of the tertiary references teaches why one of ordinary skill would be motivated to choose the human HL promoter/enhancer (–1557 to +43) taught by Ameis et al as a promoter/enhancer of interest, i.e. hepatic lipase gene in the study of importance of HL transcription. Dichek et al teach at last sentence of the abstract "HL can act as a ligand to remove apoB-containing lipoproteins from plasma" and also teach relationship between HL and apoA1. Also note columns 1-2 of the '859 patent for relationship between estrogen and lipid metabolism. Also note Materials and Methods at page 22777-8, and the last paragraph of Norris et al. As for claim 11, Norris et al teach that multi-well plates could be used in screening assay involving detection of luciferase activity; note 2nd paragraph at page 22778 and Fig. 2.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make and use the claimed invention with reasonable expectation of success since all of the necessary components of the claimed transformed cell are taught by the prior art. One of ordinary skill would have been motivated to make and use in screening

compound regulating the hepatic lipase gene promoter since Harnish et al along with Dichek et al suggest that regulating the hepatic lipase gene would be a good target in preventing heart diseases and other lipid-metabolism-related diseases in menopausal women.

Applicant argues that p300 and CBP expressing vector of the cited art and "C/EBP transcription factor" expressing vector recited in instant base claims are different and the Office's obviousness analysis does not give any connection between HL promoter and ER, thus the art as a whole would not give one in ordinary skill motivation to arrive at the instantly claimed invention with a reasonable expectation of success. Applicant's arguments have been fully considered but found unpersuasive for the following reasons.

In response to applicant argument that C/EBP transcription factor is not taught, the Office cites Landschultz et al., (CA of IDS filed on 03/17/04) or Birkenmeier et al., (CB of IDS filed on 03/17/04two IDS) in order to provide the evidence that the vector encoding the transcription factor, C/EBP has been known well before the effective filing date of the instant application.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941

(Fed. Cir. 1992). In this case, the instant claims are drawn to a recombinant cell per se with three very commonly used vectors encoding two proteins and a known- promoter linked to known reporter and one of ordinary skill in the art is motivated to use such cells in screening useful by which compound activates and repress transcription.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 03/17/2004 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment also necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

MISOOK YU, Ph.D.
Examiner
Art Unit 1642